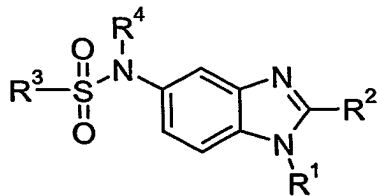


What is claimed is:

1. A compound of Formula I or a pharmaceutically acceptable salt thereof:



I

wherein

- $R^1$  is selected from  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $R^5R^6N-C_{1-6}$ alkyl,  $R^5O-C_{1-6}$ alkyl,  $R^5C(=O)N(-R^6)-C_{1-6}$ alkyl,  $R^5R^6NS(=O)_2-C_{1-6}$ alkyl,  $R^5CS(=O)_2N(-R^6)-C_{1-6}$ alkyl,  $R^5R^6NC(=O)N(-R^7)-C_{1-6}$ alkyl,  $R^5R^6NS(=O)_2N(R^7)-C_{1-6}$ alkyl,  $C_{6-10}$ aryl- $C_{1-6}$ alkyl,  $C_{6-10}$ aryl- $C(=O)-C_{1-6}$ alkyl,  $C_{3-10}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocyclyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocyclyl- $C(=O)-C_{1-6}$ alkyl,  $C_{1-10}$ hydrocarbylamino,  $R^5R^6N-$ ,  $R^5O-$ ,  $R^5C(=O)N(-R^6)-$ ,  $R^5R^6NS(=O)_2-$ ,  $R^5CS(=O)_2N(-R^6)-$ ,  $R^5R^6NC(=O)N(-R^7)-$ ,  $R^5R^6NS(=O)_2N(R^7)-$ ,  $C_{6-10}$ aryl,  $C_{6-10}$ aryl- $C(=O)-$ ,  $C_{3-10}$ cycloalkyl,  $C_{4-8}$ cycloalkenyl,  $C_{3-6}$ heterocyclyl and  $C_{3-6}$ heterocyclyl- $C(=O)-$ ; wherein said  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $C_{6-10}$ aryl- $C_{1-6}$ alkyl,  $C_{6-10}$ aryl- $C(=O)-C_{1-6}$ alkyl,  $C_{3-10}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocyclyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocyclyl- $C(=O)-C_{1-6}$ alkyl,  $C_{1-10}$ hydrocarbylamino,  $C_{6-10}$ aryl,  $C_{6-10}$ aryl- $C(=O)-$ ,  $C_{3-10}$ cycloalkyl,  $C_{4-8}$ cycloalkenyl,  $C_{3-6}$ heterocyclyl or  $C_{3-6}$ heterocyclyl- $C(=O)-$  used in defining  $R^1$  is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and  $-NR^5R^6$ ;

- $R^2$  is selected from  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $C_{3-10}$ cycloalkyl,  $C_{3-10}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl,  $R^5R^6N-$ ,  $C_{3-5}$ heteroaryl,  $C_{6-10}$ aryl and  $C_{3-6}$ heterocycloalkyl, wherein said  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $C_{3-8}$ cycloalkyl,  $C_{3-8}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl,  $C_{3-5}$ heteroaryl,  $C_{6-10}$ aryl or  $C_{3-6}$ heterocycloalkyl used in defining  $R^2$  is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and  $-NR^5R^6$ ;



C<sub>3-6</sub>heterocycloalkyl-C<sub>1-4</sub>alkyl, C<sub>4-6</sub>cycloalkenyl, C<sub>3-5</sub>heteroaryl, R<sup>5</sup>R<sup>6</sup>N-, and phenyl used in defining R<sup>2</sup> is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy and -NR<sup>5</sup>R<sup>6</sup>;

R<sup>3</sup> is selected from -H, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>3-6</sub>cycloalkyl, C<sub>3-</sub>

- 5 heterocycloalkyl,  $\text{R}^9-\text{N}(\text{R}^8)_2$  and  $\text{R}^8-\text{O}-\text{Z}$  optionally substituted with one or more groups selected from C<sub>1-6</sub>alkyl and halogen;
- each of R<sup>8</sup> and R<sup>9</sup> is independently selected from -H, C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>3-6</sub>cycloalkyl, C<sub>3-6</sub>cycloalkyl-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>heterocyclyl and C<sub>3-6</sub>heterocyclyl-C<sub>1-6</sub>alkyl, wherein said C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>3-6</sub>cycloalkyl, C<sub>3-6</sub>cycloalkyl-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>heterocyclyl, C<sub>3-6</sub>heterocyclyl-C<sub>1-6</sub>alkyl and a divalent C<sub>1-6</sub>group that together with another divalent group selected from R<sup>8</sup> and R<sup>9</sup> forms a portion of a ring, wherein said C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>3-6</sub>cycloalkyl, C<sub>3-6</sub>cycloalkyl-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>heterocyclyl and C<sub>3-6</sub>heterocyclyl-C<sub>1-6</sub>alkyl, wherein said C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>3-6</sub>cycloalkyl, C<sub>3-6</sub>cycloalkyl-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>heterocyclyl, C<sub>3-6</sub>heterocyclyl-C<sub>1-6</sub>alkyl or divalent C<sub>1-6</sub>group are optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy and -NR<sup>5</sup>R<sup>6</sup>; and R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are independently selected from -H and C<sub>1-3</sub>alkyl.

3. A compound as claimed claim 1,
- 20 wherein R<sup>1</sup> is selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, phenyl-C<sub>1-4</sub>alkyl, C<sub>3-10</sub>cycloalkyl-C<sub>1-4</sub>alkyl, C<sub>4-6</sub>cycloalkenyl-C<sub>1-4</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>3-10</sub>cycloalkyl, C<sub>3-6</sub>heterocycloalkyl-C<sub>1-4</sub>alkyl, and C<sub>4-6</sub>cycloalkenyl, wherein said C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, phenyl-C<sub>1-4</sub>alkyl, C<sub>3-10</sub>cycloalkyl-C<sub>1-4</sub>alkyl, C<sub>4-6</sub>cycloalkenyl-C<sub>1-4</sub>alkyl, C<sub>6-10</sub>aryl, C<sub>3-10</sub>cycloalkyl, C<sub>3-6</sub>heterocycloalkyl-C<sub>1-4</sub>alkyl, and C<sub>4-6</sub>cycloalkenyl used in defining R<sup>1</sup> is optionally substituted by one or more groups selected from halogen, methoxy, ethoxy, methyl, ethyl, hydroxy, and -NR<sup>5</sup>R<sup>6</sup>;
- 25 R<sup>2</sup> is selected from C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>3-6</sub>cycloalkyl and C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl, wherein said C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>3-6</sub>cycloalkyl and C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl used in defining R<sup>2</sup> is optionally substituted by one or more groups selected from halogen, methoxy, ethoxy, methyl, ethyl, hydroxy and -NR<sup>5</sup>R<sup>6</sup>;
- 30

$R^3$  is selected from  $C_{2-6}$ alkyl,  $C_{3-6}$ heterocycloalkyl and  $R^9-N(R^8)$  optionally substituted with one or more  $C_{1-6}$ alkyl, and;

wherein said  $C_{3-6}$ heterocycloalkyl contain at least one nitrogen ring atom and the radical of  $C_{3-6}$ heterocycloalkyl is located on the at least one nitrogen ring atom, and wherein each of  $R^8$  and  $R^9$  is independently selected from  $-H$ ,  $C_{1-6}$ alkyl, morpholinyl- $C_{1-3}$ alkyl, pyrrolidinyl- $C_{1-3}$ alkyl, and piperidinyl- $C_{1-3}$ alkyl, wherein said  $C_{1-6}$ alkyl, morpholinyl- $C_{1-3}$ alkyl, pyrrolidinyl- $C_{1-3}$ alkyl, and piperidinyl- $C_{1-3}$ alkyl are optionally substituted by one or more groups selected from halogen, methoxy, ethoxy, methyl, ethyl, hydroxy and  $-NR^5R^6$ ; and

10.  $R^4$ ,  $R^5$  and  $R^6$  are independently selected from  $-H$  and  $C_{1-3}$ alkyl.

4. A compound as claimed in claim 1, wherein

$R^1$  is selected from cyclohexylmethyl, cyclopentylmethyl, cyclobutylmethyl, cyclopropylmethyl, 4,4-difluorocyclohexanemethyl, cyclohexylethyl, cyclopentylethyl, tetrahydropyranylmethyl, tetrahydrofuranylmethyl, 1-piperidinylethyl, N-methyl-2-piperidinyl-methyl and benzyl;

$R^2$  is selected from t-butyl, n-butyl, 2-methyl-2-butyl, isopentyl, 2-methoxy-2-propyl, 2-hydroxy-propyl, trifluoromethyl, 1,1-difluoroethyl, 2,2,2-trifluoroethyl, 1-cyclopropyl-ethyl, 1-methyl-propyl, 1,1-dimethyl-propyl, 1,1-dimethyl-3-buten-1-yl, ethyl, and 2-propyl;

$R^3$  is  $C_{2-5}$ alkyl and  $R^8R^9N-$ , wherein  $R^8$  and  $R^9$  are independently selected from  $-H$ , and  $C_{1-3}$ alkyl.

5. A compound selected from:

25 *N*-[2-*tert*-Butyl-1-(cyclohexylmethyl)-1*H*-benzimidazol-5-yl]-*N,N,N'*-trimethylsulfamide;

*N*-[2-*tert*-Butyl-1-(cyclohexylmethyl)-1*H*-benzimidazol-5-yl]-*N,N'*-diethyl-*N*-methylsulfamide;

30

*N*-[1-(cyclohexylmethyl)-2-(1,1-dimethylpropyl)-1*H*-benzimidazol-5-yl]-*N,N*-dimethyl-sulfamide;

5 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methylbutane-1-sulfonamide;

*N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methyl-2-pyrrolidin-1-ylethanesulfonamide;

10 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methyl-2-morpholin-4-ylethanesulfonamide;

*N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methyl-2-piperidin-1-ylethanesulfonamide;

15 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-2-methoxy-*N*-methylethanesulfonamide;

20 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-2-[(2-hydroxyethyl)amino]-*N*-methylethanesulfonamide;

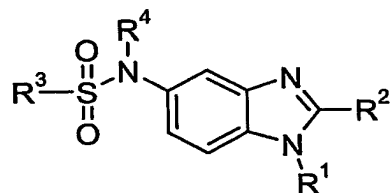
2-(2-Aminoethoxy)-*N*-[2-*tert*-butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methylethanesulfonamide;

25 *N*-[2-*tert*-Butyl-1-(tetrahydro-2*H*-pyran-4-ylmethyl)-1*H*-benzimidazol-5-yl]-*N*-methylethylenesulfonamide;

*N*-{2-*tert*-Butyl-1-[(4,4-difluorocyclohexyl)methyl]-1*H*-benzimidazol-5-yl}-*N*-methylbutane-1-sulfonamide;

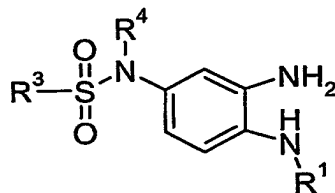
30 *N*-{2-*tert*-Butyl-1-[(4,4-difluorocyclohexyl)methyl]-1*H*-benzimidazol-5-yl}-*N*-methyl-2-piperidin-1-ylethanesulfonamide and pharmaceutically acceptable salts thereof.

6. A compound according to any one of claims 1-5 for use as a medicament.
7. The use of a compound according to any one of claims 1-5 in the manufacture  
5 of a medicament for the therapy of pain.
8. The use of a compound according to any one of claims 1-5 in the manufacture of a medicament for the treatment of anxiety disorders.
- 10 9. The use of a compound according to any one of claims 1-5 in the manufacture of a medicament for the treatment of cancer, multiple sclerosis, Parkinson's disease, Huntington's chorea, Alzheimer's disease, gastrointestinal disorders and cardiovascular disorders.
- 15 10. A pharmaceutical composition comprising a compound according to any one of claims 1-5 and a pharmaceutically acceptable carrier.
11. A method for the therapy of pain in a warm-blooded animal, comprising the step of administering to said animal in need of such therapy a therapeutically effective  
20 amount of a compound according to any one of claims 1-5.
12. A method for preparing a compound of Formula I,



**I**

- 25 comprising the step of reacting a compound of Formula II,



## II

with a compound of  $R^2C(=O)X$ , in the presence of a base and optionally a coupling reagent, followed by treatment by an acid;  
wherein

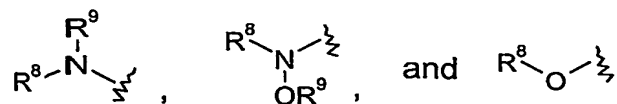
5 X is selected from Cl, Br, F and OH;

$R^1$  is selected from  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $R^5R^6N-C_{1-6}$ alkyl,  $R^5O-C_{1-6}$ alkyl,  $R^5C(=O)N(-R^6)-C_{1-6}$ alkyl,  $R^5R^6NS(=O)_2-C_{1-6}$ alkyl,  $R^5CS(=O)_2N(-R^6)-C_{1-6}$ alkyl,  $R^5R^6NC(=O)N(-R^7)-C_{1-6}$ alkyl,  $R^5R^6NS(=O)_2N(R^7)-C_{1-6}$ alkyl,  $C_{6-10}$ aryl- $C_{1-6}$ alkyl,  $C_{6-10}$ aryl- $C(=O)-C_{1-6}$ alkyl,  $C_{3-10}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocyclyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocyclyl- $C(=O)-C_{1-6}$ alkyl,  $C_{1-10}$ hydrocarbylamino,  $R^5R^6N-$ ,  $R^5O-$ ,  $R^5C(=O)N(-R^6)-$ ,  $R^5R^6NS(=O)_2-$ ,  $R^5CS(=O)_2N(-R^6)-$ ,  $R^5R^6NC(=O)N(-R^7)-$ ,  $R^5R^6NS(=O)_2N(R^7)-$ ,  $C_{6-10}$ aryl,  $C_{6-10}$ aryl- $C(=O)-$ ,  $C_{3-10}$ cycloalkyl,  $C_{4-8}$ cycloalkenyl,  $C_{3-6}$ heterocyclyl and  $C_{3-6}$ heterocyclyl- $C(=O)-$ ; wherein said  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $C_{6-10}$ aryl- $C_{1-6}$ alkyl,  $C_{6-10}$ aryl- $C(=O)-C_{1-6}$ alkyl,  $C_{3-10}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocyclyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocyclyl- $C(=O)-C_{1-6}$ alkyl,  $C_{1-10}$ hydrocarbylamino,  $C_{6-10}$ aryl,  $C_{6-10}$ aryl- $C(=O)-$ ,  $C_{3-10}$ cycloalkyl,  $C_{4-8}$ cycloalkenyl,  $C_{3-6}$ heterocyclyl or  $C_{3-6}$ heterocyclyl- $C(=O)-$  used in defining  $R^1$  is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and  $-NR^5R^6$ ;

$R^2$  is selected from  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $C_{3-10}$ cycloalkyl,  $C_{3-10}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl,  $R^5R^6N-$ ,  $C_{3-6}$ heteroaryl,  $C_{6-10}$ aryl and  $C_{3-6}$ heterocycloalkyl, wherein said  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $C_{3-8}$ cycloalkyl,  $C_{3-8}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl,  $C_{3-6}$ heteroaryl,  $C_{6-10}$ aryl or  $C_{3-6}$ heterocycloalkyl used in defining  $R^2$  is optionally substituted by one or more groups selected from halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and  $-NR^5R^6$ ;

wherein  $R^5$ ,  $R^6$  and  $R^7$  are independently selected from  $-H$ ,  $C_{1-6}$ alkyl,  $C_{2-6}$ alkenyl,  $C_{2-6}$ alkynyl, and a divalent  $C_{1-6}$ group that together with another divalent  $R^5$ ,  $R^6$  or  $R^7$  forms a portion of a ring;

$R^3$  is selected from  $-H$ ,  $C_{1-10}$ alkyl,  $C_{2-10}$ alkenyl,  $C_{2-10}$ alkynyl,  $C_{3-10}$ cycloalkyl,  $C_{3-10}$ cycloalkyl- $C_{1-6}$ alkyl,  $C_{4-8}$ cycloalkenyl- $C_{1-6}$ alkyl,  $C_{3-6}$ heterocycloalkyl,



optionally substituted with one or more

groups selected from C<sub>1-6</sub>alkyl, halogen, amino and C<sub>1-6</sub>alkoxy;

each of R<sup>8</sup> and R<sup>9</sup> is independently selected from -H, C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, C<sub>3-10</sub>cycloalkyl, C<sub>3-10</sub>cycloalkyl-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>heterocyclyl, C<sub>6-10</sub>aryl,

5 C<sub>3-6</sub>heterocylcyl-C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl-C<sub>1-6</sub>alkyl, and a divalent C<sub>1-6</sub>group that together with another divalent group selected from R<sup>8</sup> and R<sup>9</sup> forms a portion of a ring,

wherein said C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, C<sub>3-10</sub>cycloalkyl, C<sub>3-10</sub>cycloalkyl-C<sub>1-6</sub>alkyl, C<sub>3-6</sub>heterocyclyl, C<sub>6-10</sub>aryl, C<sub>3-6</sub>heterocylcyl-C<sub>1-6</sub>alkyl, C<sub>6-10</sub>aryl-C<sub>1-6</sub>alkyl, or divalent C<sub>1-6</sub>group is optionally substituted by one or more groups selected from

10 halogen, cyano, nitro, methoxy, ethoxy, methyl, ethyl, hydroxy, and -NR<sup>5</sup>R<sup>6</sup>; and

R<sup>4</sup> is selected from -H, C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, C<sub>3-10</sub>cycloalkyl, C<sub>3-10</sub>cycloalkyl-C<sub>1-6</sub>alkyl, and C<sub>4-8</sub>cycloalkenyl-C<sub>1-6</sub>alkyl.